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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,157	01/28/2004	Thomas P. Loughran JR.	USF-T190XC1	5993
23557	7590	01/30/2006	EXAMINER	
SALIWANCHIK LLOYD & SALIWANCHIK A PROFESSIONAL ASSOCIATION PO BOX 142950 GAINESVILLE, FL 32614-2950			YAO, LEI	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 01/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/766,157

Applicant(s)

LOUGHRAN ET AL.

Examiner

Lei Yao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 August 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,4,6 and 19-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,4,6 and 19-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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***DETAILED ACTION***

The Amendment filed on 11/4/05 in response to the previous Non-Final Office Action (8/1/05) is acknowledged and has been entered.

Claims 2-3, 5, 7-18 have been cancelled. Claim 1 has been amended. Claims 19-24 have been added.

Claims 1, 4, 6, 19-24 are pending and under consideration.

**The text of those sections of Title 35, U.S.Code not included in this action can be found in the prior Office Action.**

The following office action contains NEW GROUNDS of rejection.

**Rejections Withdrawn**

1. The rejection of claims 1-2 under 35 USC § 102 as being anticipated by Smyth et al., (J leukoc Biol, vol 57, page 88-93, 1995) is withdrawn in view of the cancellation to the claims and applicants argument.
2. The rejection of claims 1, 4-6 under 35 USC § 103 as being anticipated by being unpatentable over Warrington et al., (US Patent Application, US2001/0044104, Nov, 22 2001) in view of Robertson et al., (Exp Hematol, vol 24, page 406-15, Feb, 1996) and Lamy et al., (Blood, vol 92, page 4771-4777, Dec, 1998) is withdrawn in view of the amendment to the claims.

**The following are NEW GROUNDS of rejection**

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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***As drawn to new matter***

Claims 1, 20, and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is noted that the claims 20 and 22 are as newly added claims reciting a method for screening, detecting, diagnosing large granular Lymphocyte (LGL) leukemia comprising detecting upregulated expression of Granzyme in leukemic LGL cell compared to normal LGL cell or non-LGL cell, which is not supported by instant specification. Instant specification as filed, although providing sample from leukemic LGL, normal cell, normal sera, and activated PBMC, does not provide sufficient support for the instant claims reciting "normal LGL cell".

***Claim Rejections under 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 4, 6, 19-24 are rejected under 35 U.S.C. 102(a) as being anticipated Kothapalli et al., (Int J Oncol, vol 22, page 33-39, Jan 2003).

The set of claims is drawn to a method of screening, detecting, or diagnosing LGL leukemia by detecting upregulated expression of granzymes in peripheral blood sample, wherein assaying levels of RNA by microarray and levels of protein by Western blot assay.

Kothapalli et al., disclose a method of screening, detecting, or diagnosing LGL leukemia by detecting upregulated expression of granzymes comprising granzyme B and H in peripheral blood sample. Kothapalli et al., disclose that the RNA levels of granzymes are upregulated in the sample from

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a patient having LGL leukemia assaying by Northern blot (figure 2A, page 36). Kothapalli et al., also disclose that upregulated gene expression of the granzymes is confirmed by Western blot (figure 4, page 38).

***Claim Rejections under 35 USC § 103***

Claims 1, 4, 6, 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over in Warrington et al., (US Patent Application, US2001/0044104, Nov, 22 2001) in view of Lamy et al., (Blood, vol 92, page 4771-4777, Dec, 1998) and Smyth et al., (J leukoc Biol, vol 57, page 88-93, 1995).

Warrington et al., teach a method for screening, detecting, or diagnosing a lymphocytic leukemia by gene expression profile obtained from microarray (paragraph 52, 54, and 95). Warrington et al., teach differential expression of genes in a disease and normal tissue as an example (page 11-13). Warrington et al., also teach diagnosing and monitoring disease states by the gene expression profile.

Warrington et al., do not teach that gene expression profile for large granular lymphocytes (LGL) leukemia.

Lamy et al., teach a characteristic of LGL leukemia. Lamy et al., teach a gene expression by LGL leukemia cells isolated from peripheral blood mononuclear cells derived from patient with LGL leukemia (page 4773, figure 1 and table 2).

Smyth et al., teach a method of determining LGL by detecting the expression of RNA and protein of Granzyme B. Smyth et al., teach a method of comparing the levels of gene expression between LGL and high-density small lymphocytes. Smyth et al., teach detecting levels of RNA by Northern analysis (page 89, col 2 and page 91, fig 4) and by Western analysis (page 89, col 1, and fig 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of detecting, diagnosing, screening of LGL leukemia by assaying the levels of gene expression of Granzyme taught by the references. One of ordinary skill in the art would have been motivated to screen LGL leukemia in a subject by determining the expression levels of all Granzymes comprising A, B, H and K by applying the Smyth et al., and Lamy et al., method to the method taught by Warrington et al. One of ordinary skill in the art would have been motivated with a

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reasonable expectation of success to apply the teachings of Lamy et al., and Smyth et al., to the teaching of Warrington et al., One of ordinary skill in the art would have been motivated with a reasonable expectation of success to diagnose, screen, or detect LGL leukemia by determining the levels of specific gene expressions comprising the levels of Granzymes because Warrington et al., have shown how to use the method for diseases diagnosis, Lamy et al., have shown that the gene expression are different between the normal peripheral blood and LGL leukemia cells, and Smyth et al., have shown differential expression of Granzyme B in the LGL and other lymphocytes.

### **Conclusion**

NO claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

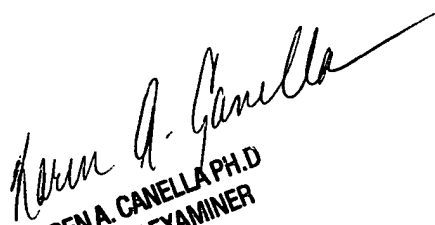
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.  
Examiner  
Art Unit 1642

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KAREN A. CANELLA PH.D.  
PRIMARY EXAMINER